FIGURE 1

```
att ccg gct tct atg gag cac tcg gga cca ggt ccg cgg cgc gcg cac tcg ctc

gct cgc cgc ccc cca gcc agc tct cgc ttc cgc gcc gcc agc cgc gcc ccg cgc

ctc ctc gct gca ccc cgc gac cta gag cca aga aag ttt gtg tgg cga gtg agg

gcc gga gag gag agc gcg ccc gcg gag tgc cgt cca gac cag cgc ggc ccc ggc

gga gag ggg agc gcc ccg agc cca ggc ggc ggc ggc tag ccc gag tcc gcg acc
                        -26                         -20
                        Met Gly Ala Ala Ala Arg Ser Leu Pro Leu Ala Phe
ccc gcc cct ccg ccc gcc atg ggc gcc gcc gcc cgc agc ctg ccg ctc gcg ttc
                    -10                             -1   1
Cys Leu Leu Leu Leu Gly Thr Leu Leu Pro Arg Ala Asp Ala Cys Ser Cys Ser
tgc ctc ctg ctg ctg ggg acg ctg ctc ccc cgg gcc gac gcc tgc agc tgc tcc
                        10                              20
Pro Val His Pro Gln Gln Ala Phe Cys Asn Ala Asp Ile Val Ile Arg Ala Lys
ccg gtg cac ccg caa cag gcg ttt tgc aat gca gac ata gtg atc agg gcc aaa
                            30                                      40
Ala Val Asn Lys Lys Glu Val Asp Ser Gly Asn Asp Ile Tyr Gly Asn Pro Ile
gca gtc aat aag aag gag gtg gac tct ggc aac gac atc tac ggc aac ccc atc
                                50
Lys Arg Ile Gln Tyr Glu Ile Lys Gln Ile Lys Met Phe Lys Gly Pro Asp Gln
aag cgg att cag tat gag atc aag cag ata aag atg ttc aag gga cct gat cag
      60                                    70
Asp Ile Glu Phe Ile Tyr Thr Ala Pro Ala Ala Ala Val Cys Gly Val Ser Leu
gac ata gag ttt atc tac aca gcc ccc gcc gct gcc gtg tgt ggg gtc tcg ctg
                80                                  90
Asp Ile Gly Gly Lys Lys Glu Tyr Leu Ile Ala Gly Lys Ala Glu Gly Asn Gly
gac att gga gga aag aag gag tat ctc att gca ggg aag gcc gag ggg aat ggc
                        100                             110
Asn Met His Ile Thr Leu Cys Asp Phe Ile Val Pro Trp Asp Thr Leu Ser Ala
aat atg cat atc acc ctc tgt gac ttc atc gtg ccc tgg gac acc ctg agt gcc
                            120                                     130
Thr Gln Lys Lys Ser Leu Asn His Arg Tyr Gln Met Gly Cys Glu Cys Lys Ile
acc cag aag aag agc ctg aac cac agg tac cag atg ggc tgt gag tgc aag atc
                                140
Thr Arg Cys Pro Met Ile Pro Cys Tyr Ile Ser Ser Pro Asp Glu Cys Leu Trp
act cga tgc ccc atg atc cca tgc tac atc tcc tct ccg gac gag tgc ctc tgg
      150                                   160
Met Asp Trp Val Thr Glu Lys Asn Ile Asn Gly His Gln Ala Lys Phe Phe Ala
atg gac tgg gtc acg gag aag aac atc aac gga cac cag gcc aag ttc ttc gcc
                170                                 180
Cys Ile Lys Arg Ser Asp Gly Ser Cys Ala Trp Tyr Arg Gly Ala Ala Pro Pro
tgc atc aag aga agc gac ggc tcc tgc gcc tgg tac cgc gga gca gca ccc ccc
                        190                 194
Lys Gln Glu Phe Leu Asp Ile Glu Asp Pro
aag cag gag ttt ctg gac atc gag gac ccg taa gca ggc cac cag gac tcc tgg

ggc caa ttg aca gtg tcc aag agt tca gac tgg tcc agc tcc gac atc cct tcc

tgg aca cag cat gaa taa a
```

FIGURE 2

```
att ccg gcc cgc cgt ccc cca ccc cgc cgc ccc gcc cgg cga att gcg ccc cgc

gcc cct ccc ctc gcg ccc ccg aga caa aga gga gag aaa gtt tgc gcg gcc gag

cgg ggc agg tga gga ggg tga gcc gcg cgg gag ggg ccc gcc tcg gcc ccg gct

cag ccc ccg ccc gcg ccc cca gcc cgc cgc cgc gag cag cgc ccg gac ccc cca
                                                  -26
                                                  Met Gly Ala Ala Ala Arg
gcg gcg gcc ccc gcc cgc cca gcc ccc cgg ccc gcc atg ggc gcc gcg gcc cgc
-20                                          -10
Thr Leu Arg Leu Ala Leu Gly Leu Leu Leu Leu Ala Thr Leu Leu Arg Pro Ala
acc ctg cgg ctg gcg ctc ggc ctc ctg ctg ctg gcg acg ctg ctt cgc ccg gcc
    -1  1                                       10
Asp Ala Cys Ser Cys Ser Pro Val His Pro Gln Gln Ala Phe Cys Asn Ala Asp
gac gcc tgc agc tgc tcc ccg gtg cac ccg caa cag gcg ttt tgc aat gca gat
              20                                    30
Val Val Ile Arg Ala Lys Ala Val Ser Glu Lys Glu Val Asp Ser Gly Asn Asp
gta gtg atc agg gcc aaa gcg gtc agt gag aag gaa gtg gac tct gga aac gac
                    40                                  50
Ile Tyr Gly Asn Pro Ile Lys Arg Ile Gln Tyr Glu Ile Lys Gln Ile Lys Met
att tat ggc aac cct atc aag agg atc cag tat gag atc aag cag ata aag atg
                        60                                      70
Phe Lys Gly Pro Glu Lys Asp Ile Glu Phe Ile Tyr Thr Ala Pro Ser Ser Ala
ttc aaa ggg cct gag aag gat ata gag ttt atc tac acg gcc ccc tcc tcg gca
                        80
Val Cys Gly Val Ser Leu Asp Val Gly Gly Lys Lys Glu Tyr Leu Ile Ala Gly
gtg tgt ggg gtc tcg ctg gac gtt gga gga aag aag gaa tat ctc att gca gga
    90                                      100
Lys Ala Glu Gly Asp Gly Lys Met His Ile Thr Leu Cys Asp Phe Ile Val Pro
aag gcc gag ggg gac ggc aag atg cac atc acc ctc tgt gac ttc atc gtg ccc
              110                                   120
Trp Asp Thr Leu Ser Thr Thr Gln Lys Lys Ser Leu Asn His Arg Tyr Gln Met
tgg gac acc ctg agc acc acc cag aag aag agc ctg aac cac agg tac cag atg
                    130                                 140
Gly Cys Glu Cys Lys Ile Thr Arg Cys Pro Met Ile Pro Cys Tyr Ile Ser Ser
ggc tgc gag tgc aag atc acg cgc tgc ccc atg atc ccg tgc tac atc tcc tcc
                        150                                     160
Pro Asp Glu Cys Leu Trp Met Asp Trp Val Thr Glu Lys Asn Ile Asn Gly His
ccg gac gag tgc ctc tgg atg gac tgg gtc aca gag aag aac atc aac ggg cac
                        170
Gln Ala Lys Phe Phe Ala Cys Ile Lys Arg Ser Asp Gly Ser Cys Ala Trp Tyr
cag gcc aag ttc ttc gcc tgc atc aag aga agt gac ggc tcc tgt gcg tgg tac
    180                                     190                 194
Arg Gly Ala Ala Pro Pro Lys Gln Glu Phe Leu Asp Ile Glu Asp Pro
cgc ggc gcg gcg ccc ccc aag cag gag ttt ctc gac atc gag gac cca taa gca

ggc ctc caa cgc ccc tgt ggc caa ctg caa aaa aag cct cca agg gtt tcg act

ggt cca gct ctg aca tcc ctt cct gga aac agc atg aat aaa aca ctc atc ccc

gga att c
```

FIGURE 3

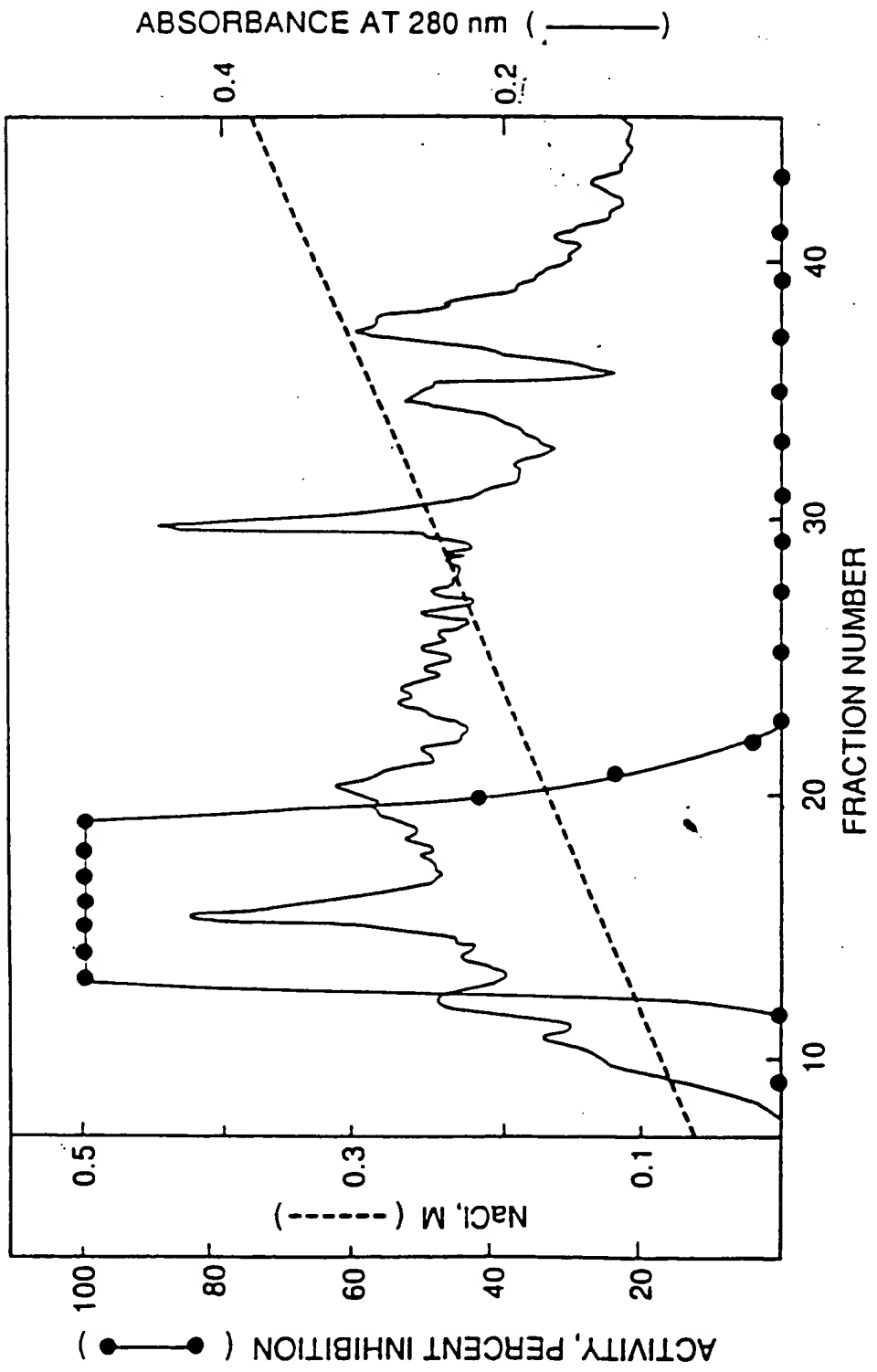

ABSORBANCE AT 280 nm (———)
0.4
0.2
40
30
20
10
FRACTION NUMBER
0.5
0.3
0.1
NaCl, M (------)
100
80
60
40
20
ACTIVITY, PERCENT INHIBITION (●——●)

FIGURE 4

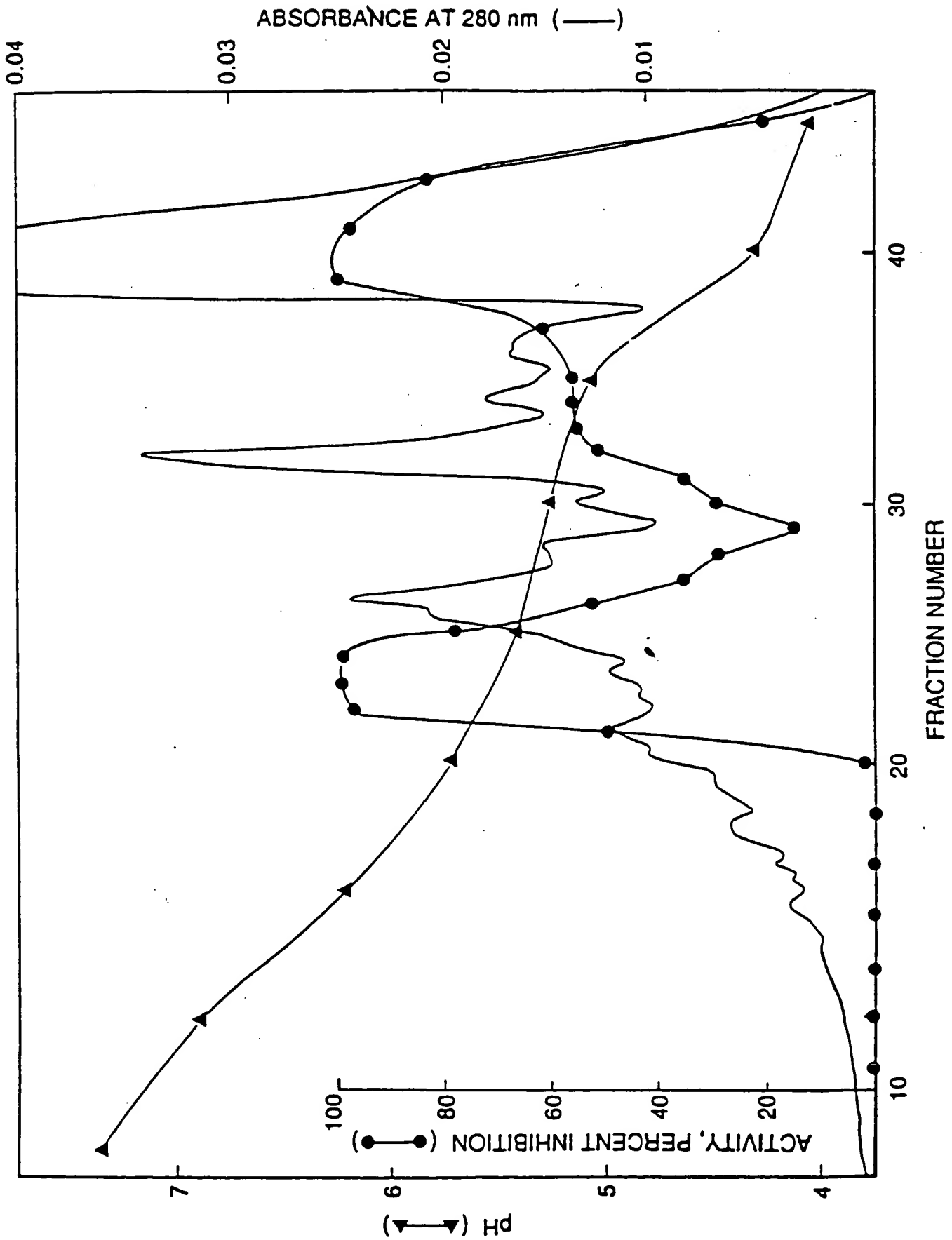

ABSORBANCE AT 280 nm (——)
0.04
0.03
0.02
0.01
FRACTION NUMBER
10
20
30
40
ACTIVITY, PERCENT INHIBITION (●—●)
100
80
60
40
20
pH (▲—▲)
7
6
5
4

FIGURE 5

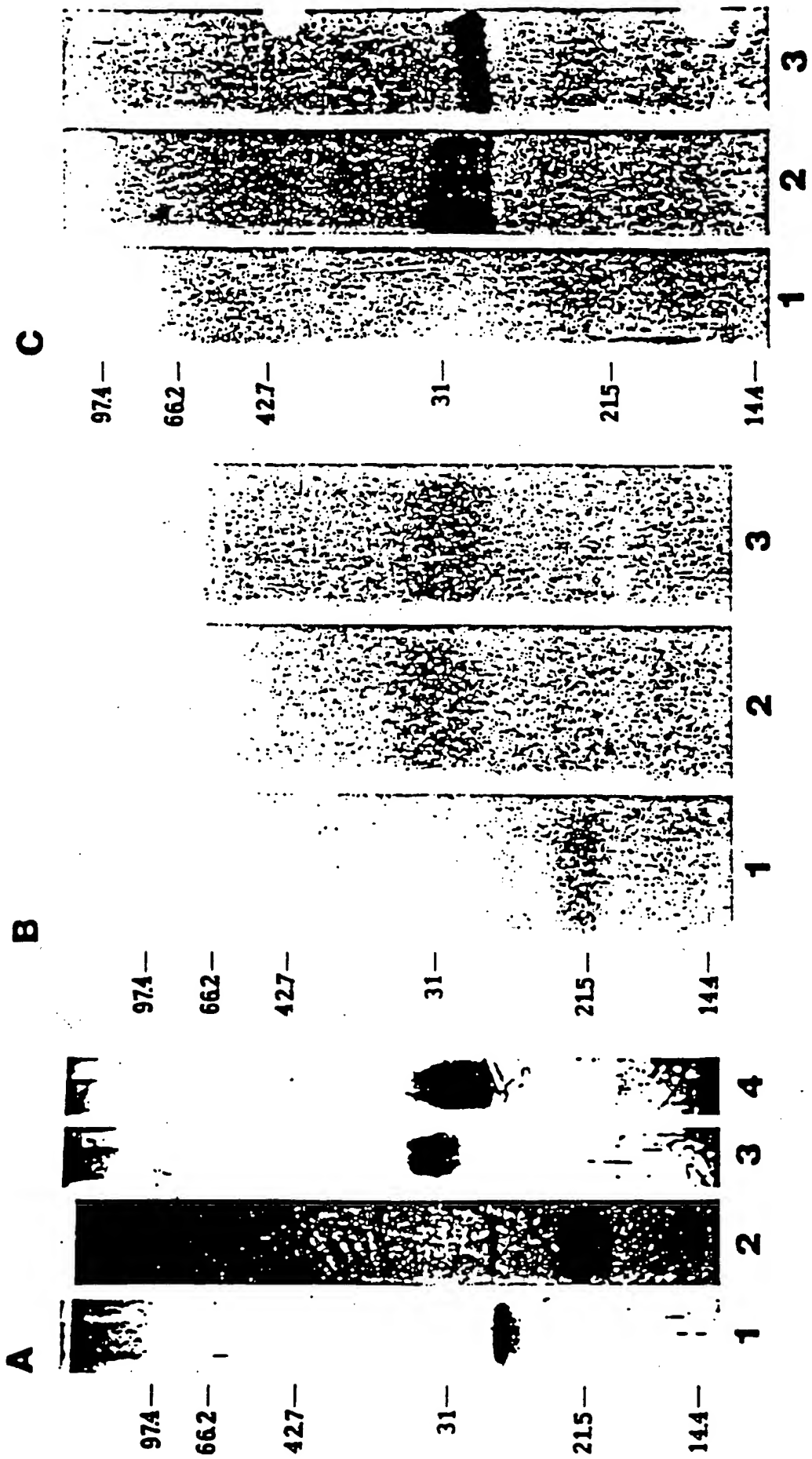


FIGURE 6

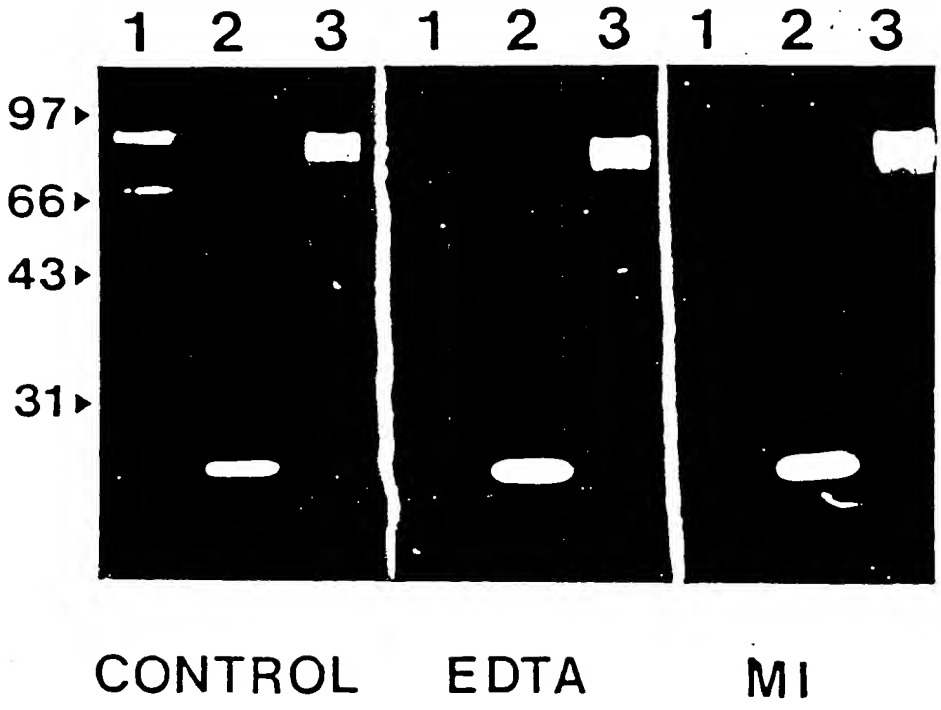
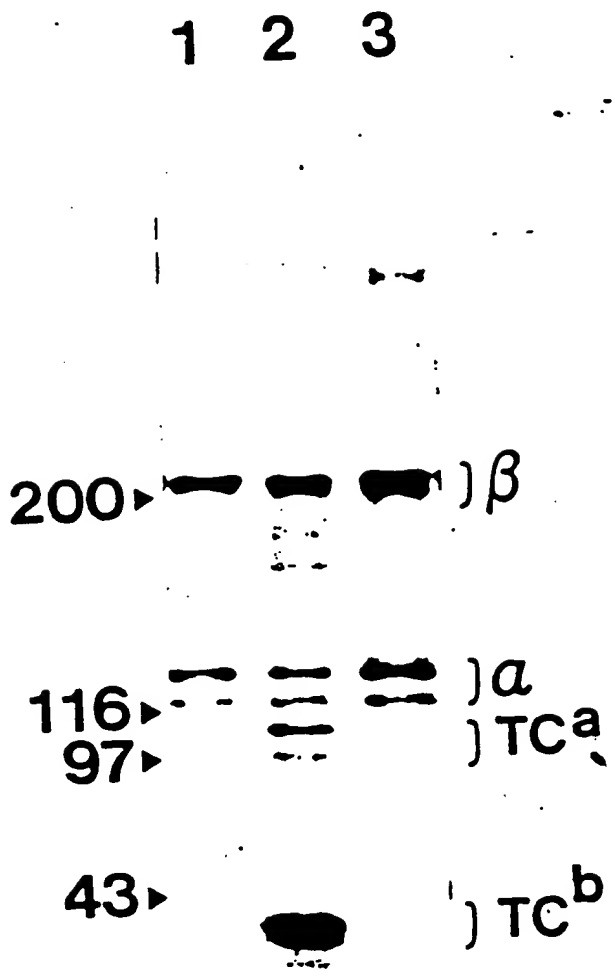


FIGURE 7



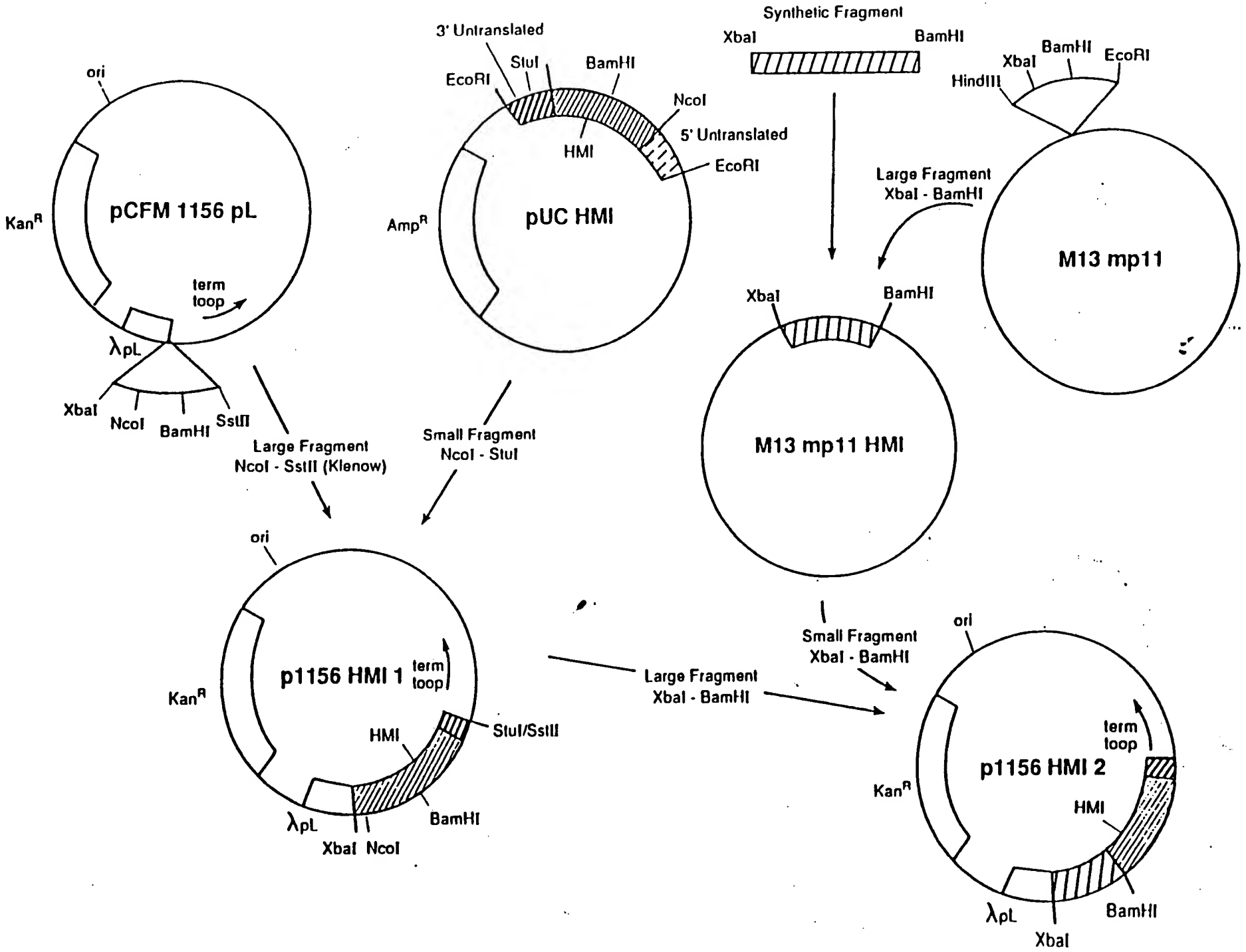

pCFM 1156 pL
ori
Kan^R
term loop
λpL
XbaI
NcoI
BamHI
SstII
3' Untranslated
StuI
EcoRI
BamHI
NcoI
5' Untranslated
EcoRI
HMI
pUC HMI
Amp^R
Synthetic Fragment
XbaI
BamHI
HindIII
XbaI
BamHI
EcoRI
M13 mp11
Large Fragment
XbaI - BamHI
XbaI
BamHI
M13 mp11 HMI
Large Fragment
NcoI - SstII (Klenow)
Small Fragment
NcoI - StuI
ori
p1156 HMI 1
term loop
Kan^R
HMI
StuI/SstII
λpL
BamHI
XbaI
NcoI
Large Fragment
XbaI - BamHI
Small Fragment
XbaI - BamHI
ori
term loop
p1156 HMI 2
Kan^R
HMI
λpL
BamHI
XbaI

FIGURE 8

FIGURE 9

```
          10          20          30          40          50          60
CTAGAAAAAA CCAAGGAGGT AATAAATAAT GTGTTCTTGT TCTCCTGTAC ACCCTCAACA
     TTTTTT GGTTCCTCCA TTATTTATTA CACAAGAACA AGAGGACATG TGGGAGTTGT

          70          80          90         100         110         120
AGCTTTTTGT AACGCTGATG TAGTTATCCG TGCAAAAGCT GTTTCTGAAA AAGAAGTTGA
TCGAAAAACA TTGCGACTAC ATCAATAGGC ACGTTTTCGA CAAAGACTTT TTCTTCAACT

         130         140         150         160
TTCTGGTAAC GACATCTACG GTAACCCGAT CAAAAG.
AAGACCATTG CTGTAGATGC CATTGGGCTA GTTTTCCTAG
```

FIGURE 10

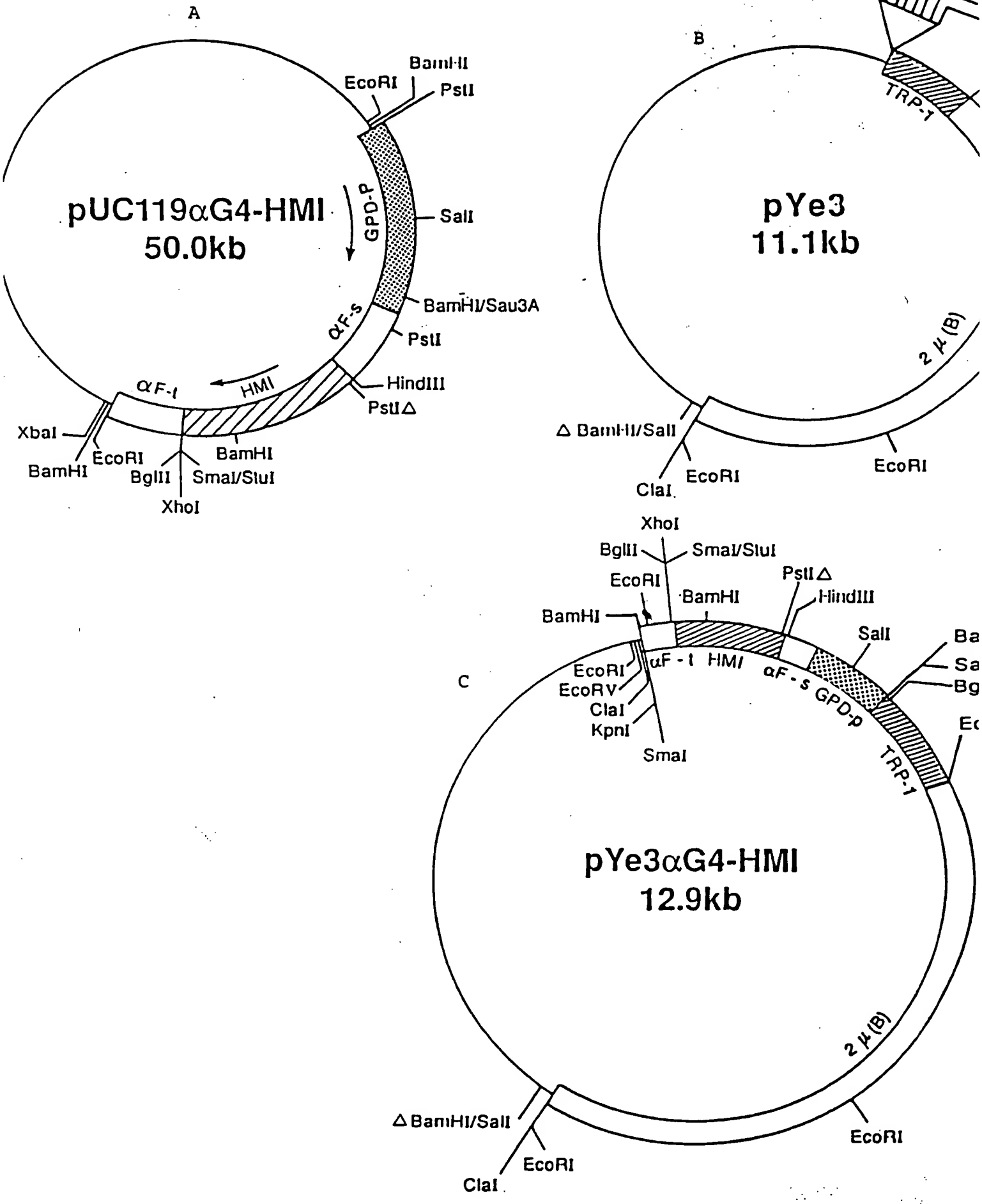

A
pUC119αG4-HMI
50.0kb
BamHI
EcoRI
PstI
SalI
GPD-P
αF-s
BamHI/Sau3A
PstI
HindIII
PstI△
αF-l
HMI
XbaI
EcoRI
BamHI
BamHI
BglII
SmaI/StuI
XhoI
B
pYe3
11.1kb
EcoRV
ClaI
EcoRI
TRP-1
2μ(B)
△ BamHI/SalI
EcoRI
ClaI
EcoRI
C
pYe3αG4-HMI
12.9kb
XhoI
BglII
SmaI/StuI
EcoRI
BamHI
PstI△
HindIII
BamHI
SalI
αF-l
HMI
αF-s
GPD-p
EcoRI
EcoRV
ClaI
KpnI
SmaI
TRP-1
2μ(B)
△ BamHI/SalI
EcoRI
ClaI
EcoRI

FIGURE 11

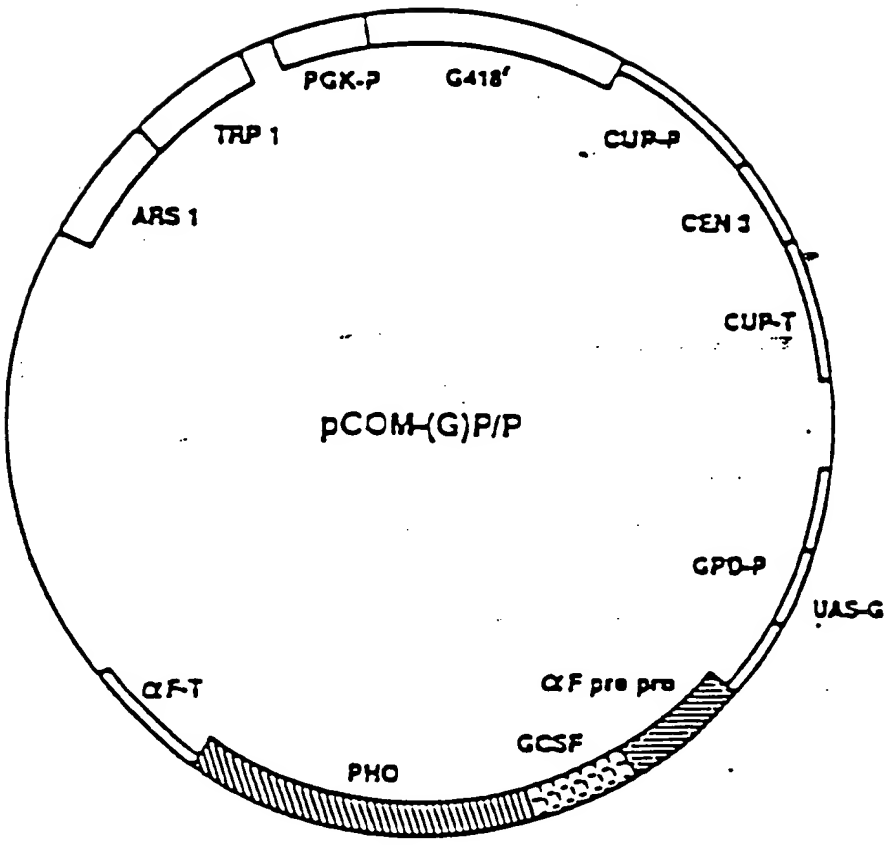

PGK-P
G418r
TRP 1
CUP-P
ARS 1
CEN 3
CUP-T
pCOM-(G)P/P
GPD-P
UAS-G
αF-T
αF pre pro
GCSF
PHO

FIGURE 12

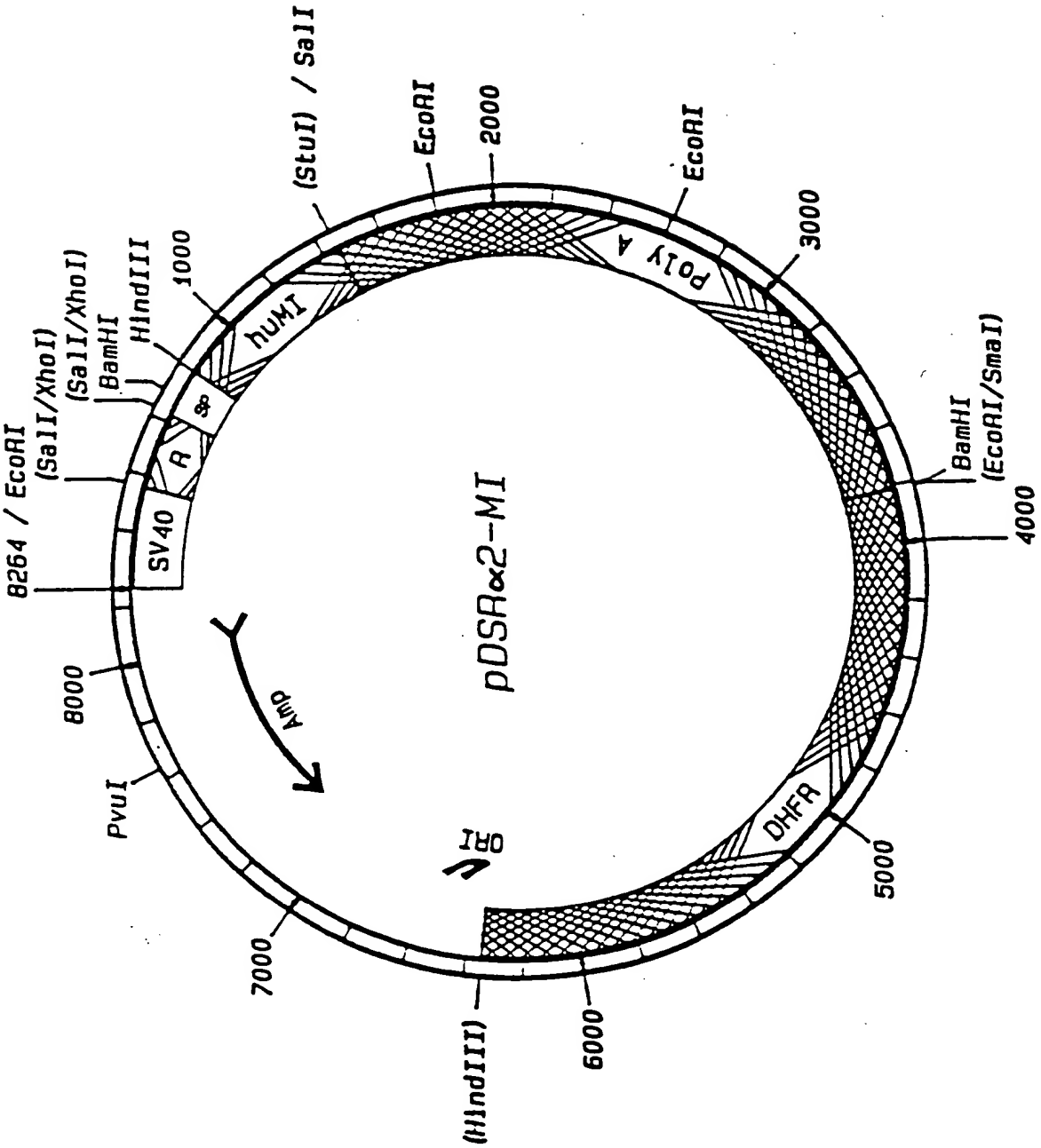

pDSRα2-MI
(StuI) / SalI
EcoRI
2000
EcoRI
3000
BamHI
(EcoRI/SmaI)
4000
5000
DHFR
6000
(HindIII)
7000
PvuI
8000
8264 / EcoRI
(SalI/XhoI)
(SalI/XhoI)
BamHI
HindIII
1000
hUMI
SV40
Poly A
Amp
ORI

FIGURE 13

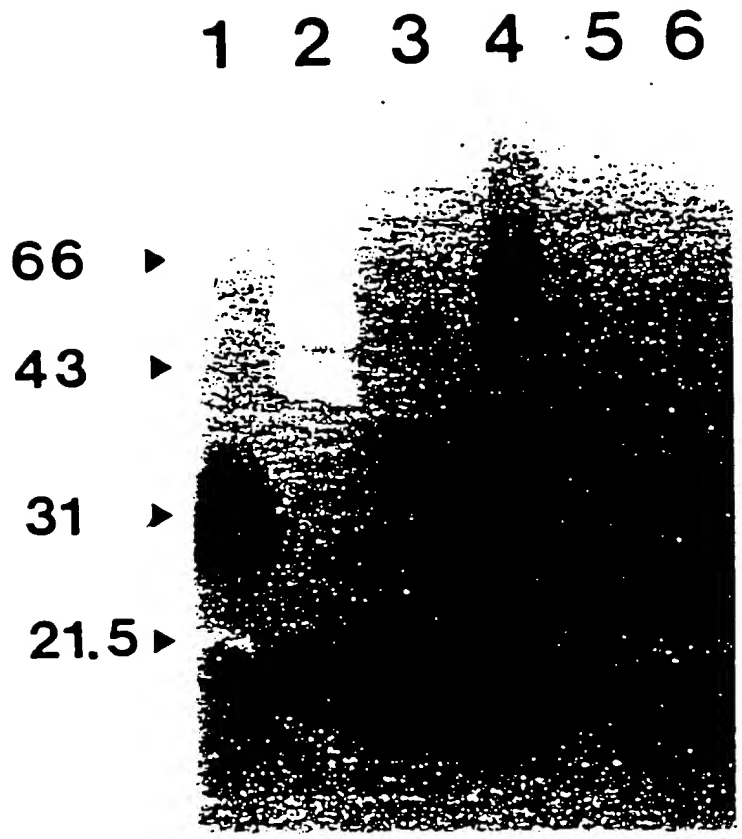


FIGURE 14

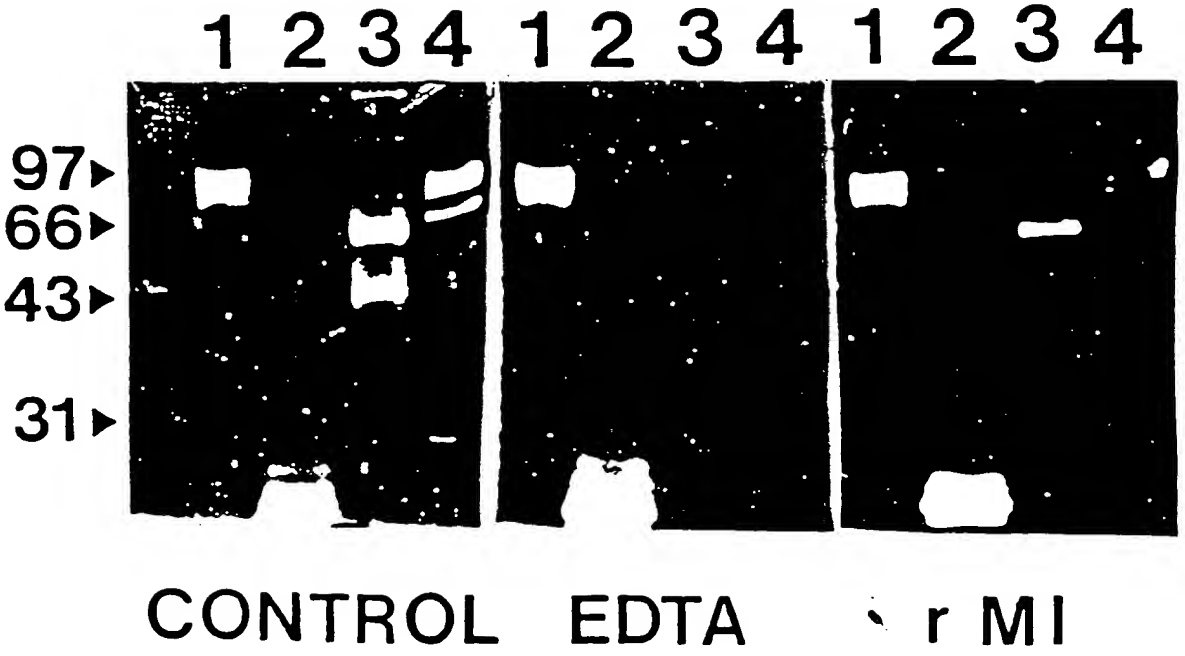


FIGURE 15

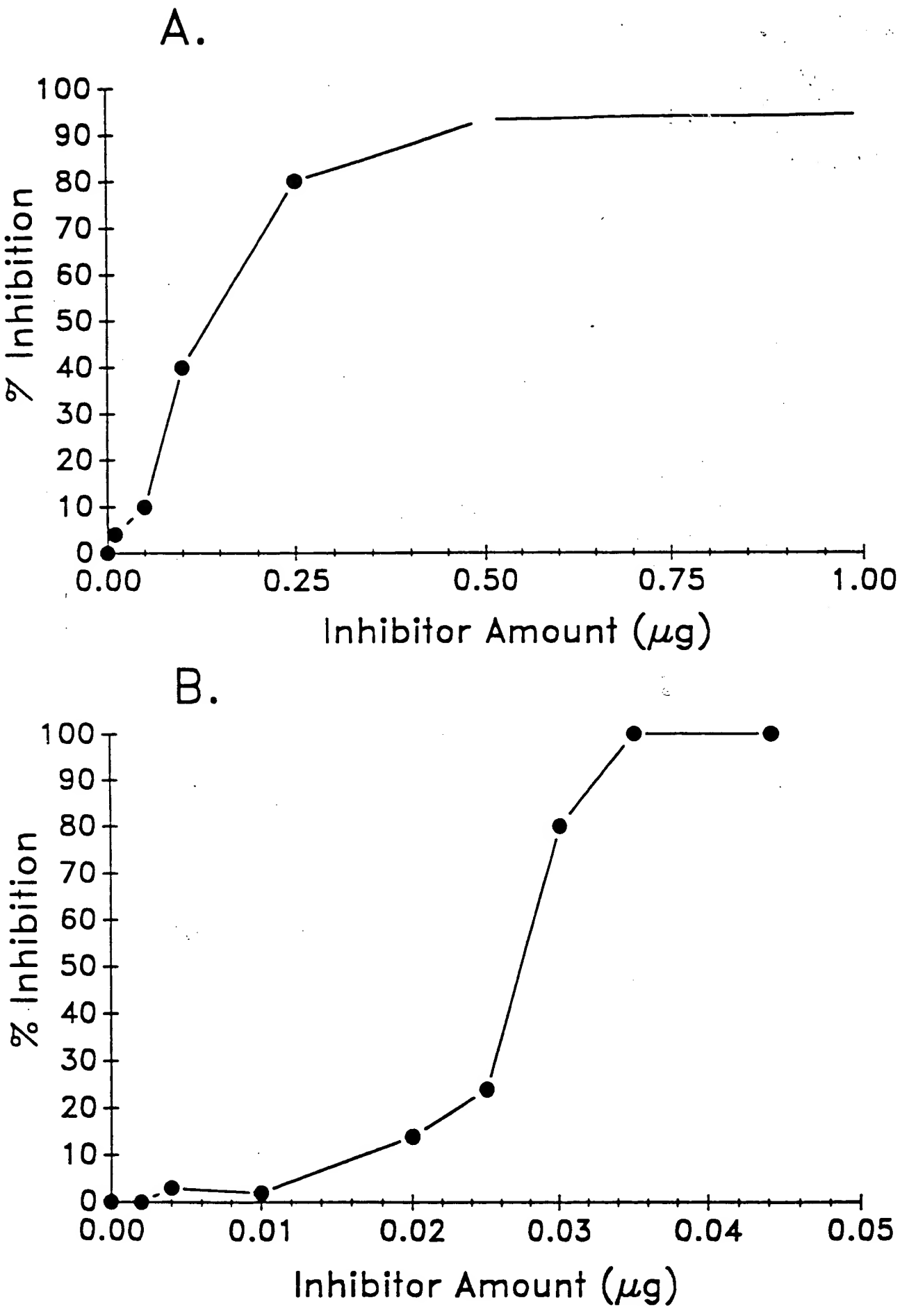

A.
100
90
80
70
60
50
40
30
20
10
0
% Inhibition
0.00
0.25
0.50
0.75
1.00
Inhibitor Amount (μg)
B.
100
90
80
70
60
50
40
30
20
10
0
% Inhibition
0.00
0.01
0.02
0.03
0.04
0.05
Inhibitor Amount (μg)

FIGURE 16

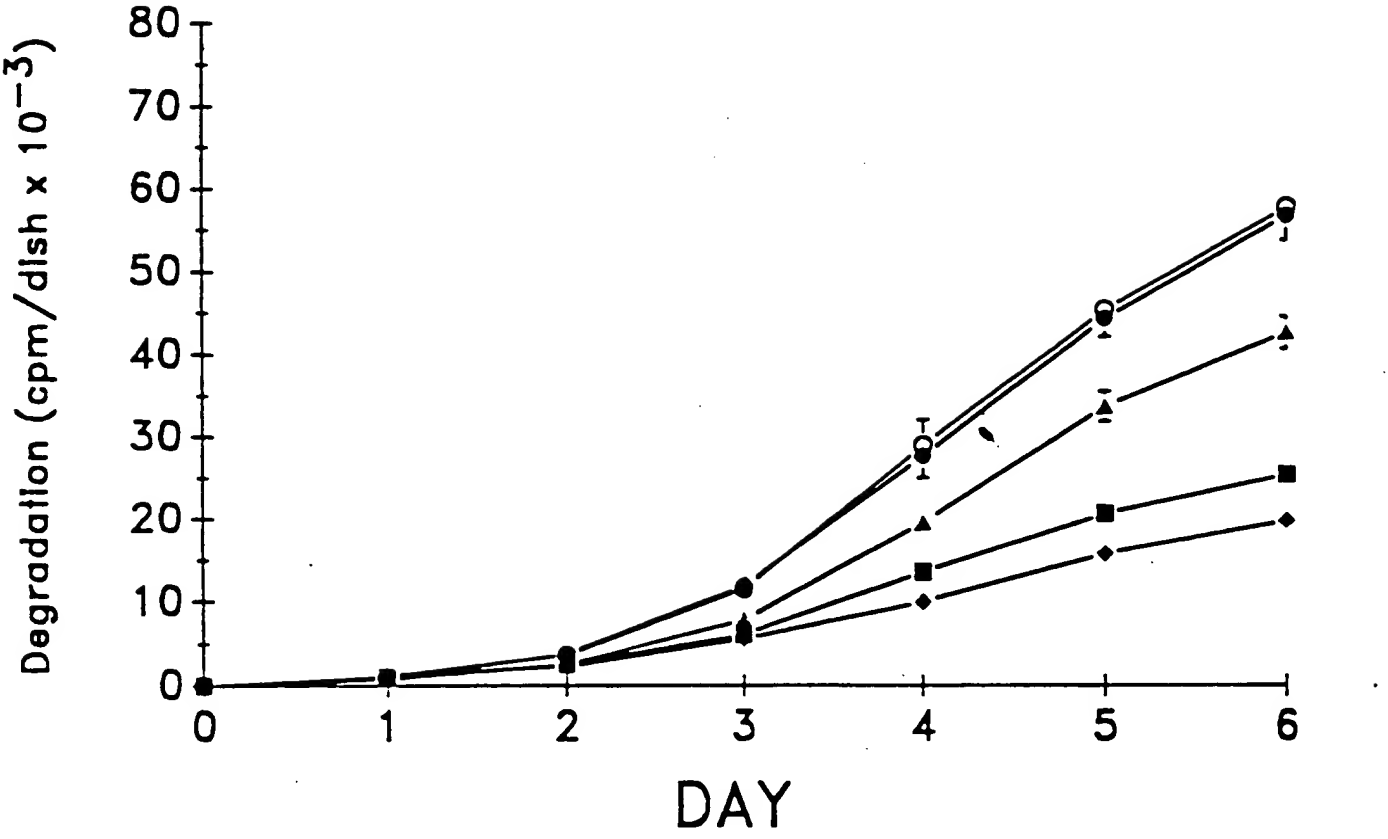


FIGURE 17

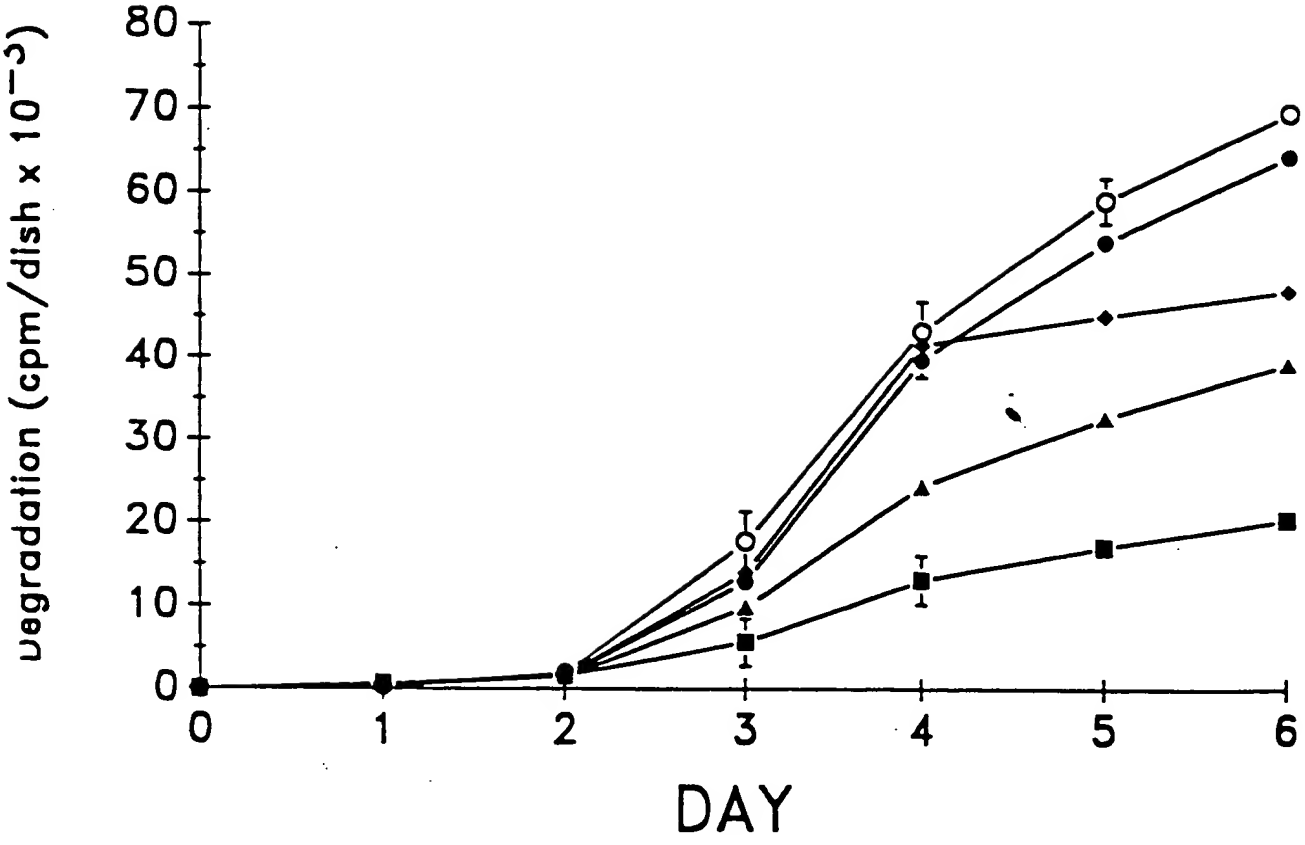


FIGURE 19

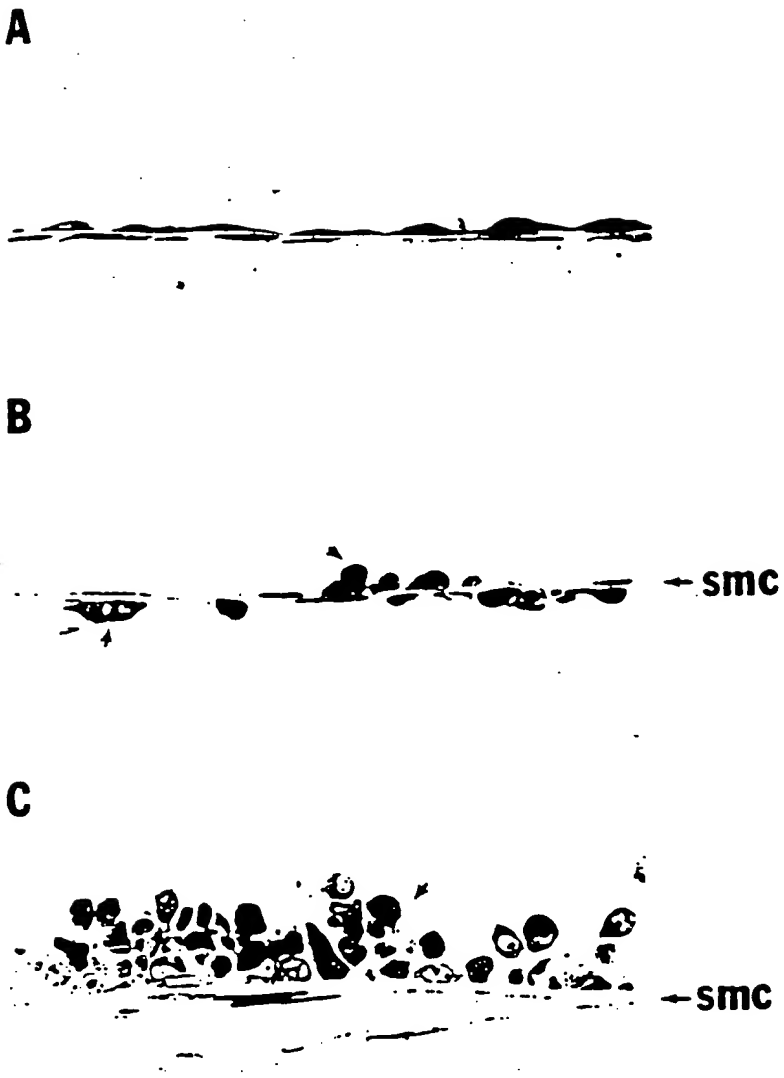


FIGURE 20

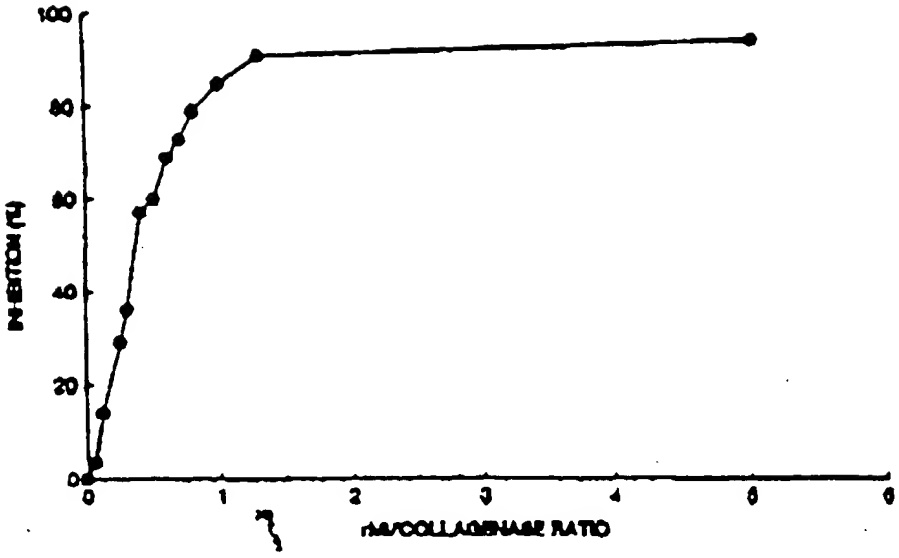


FIGURE 21

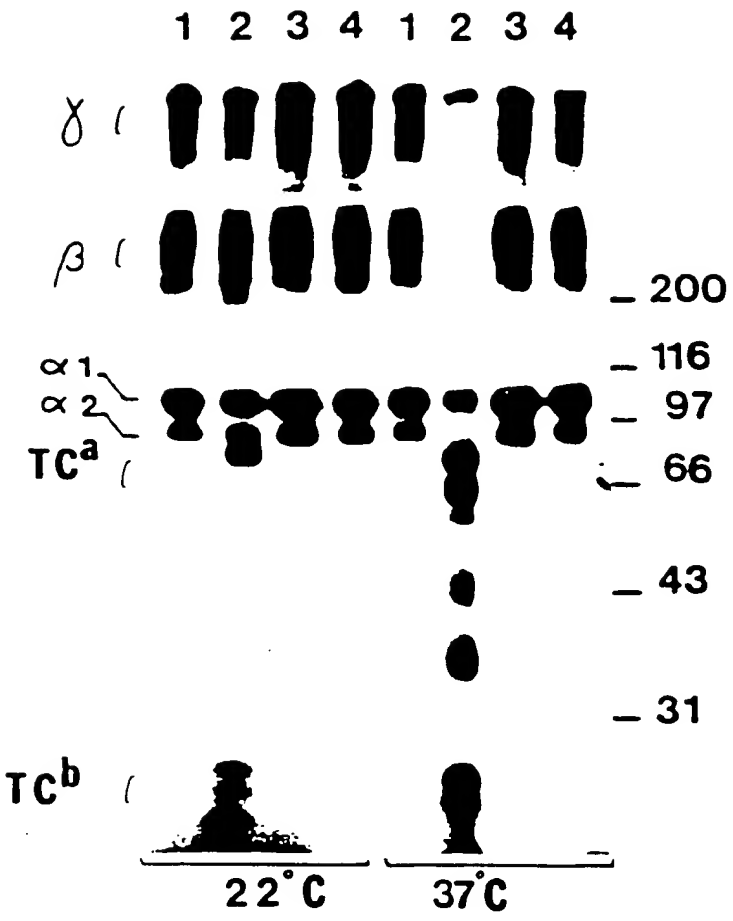


FIGURE 22

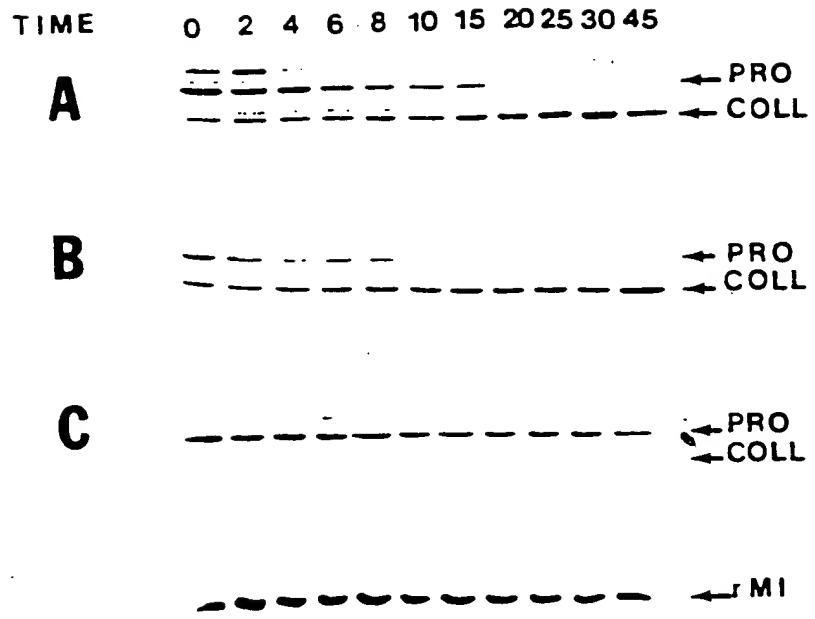


FIGURE 23

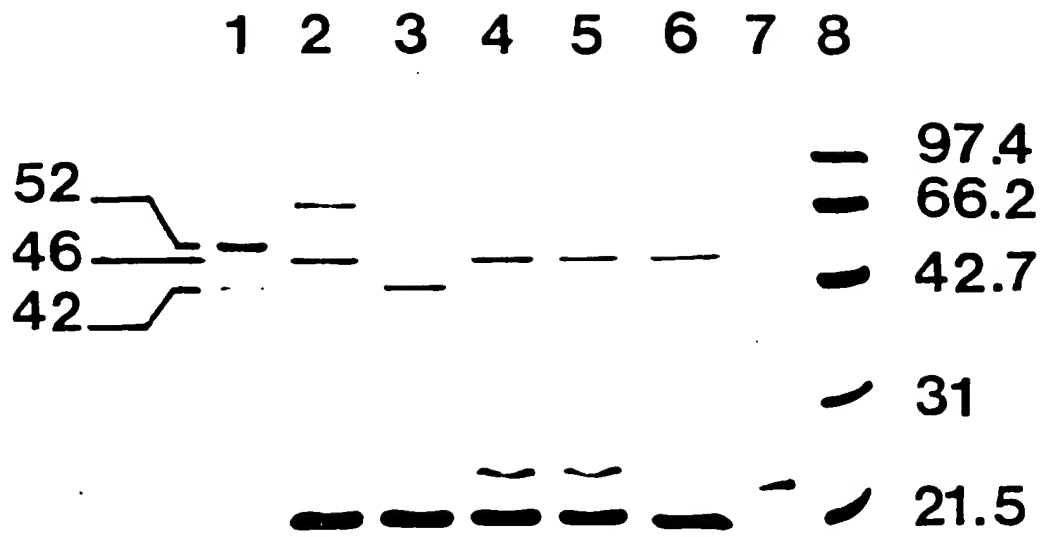


FIGURE 24


A
1 2 3 4 5 6 7 8 9 10
97
66
52
43
42
31
rMI
21
B
1 2 3 4 5 6 7 8 9
130
75
50
39
27
17

FIGURE 25

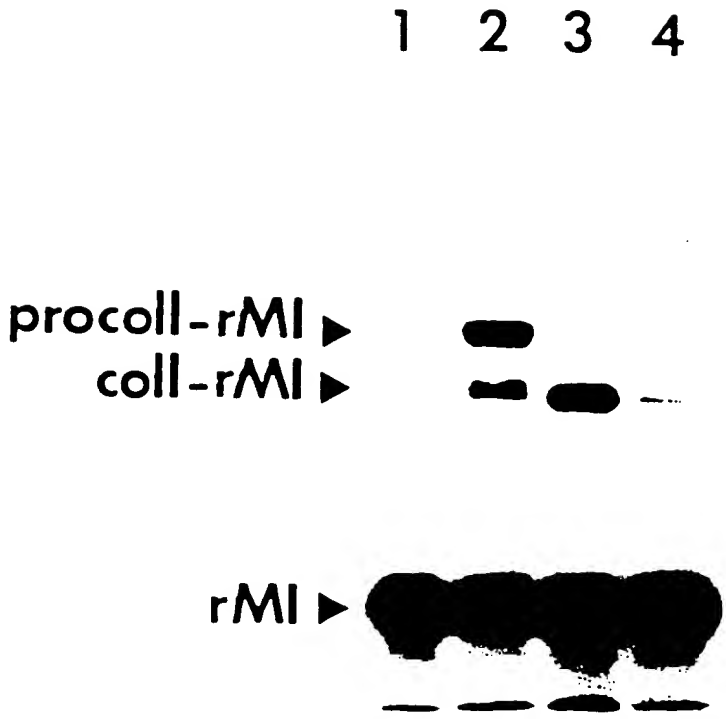


FIGURE 26

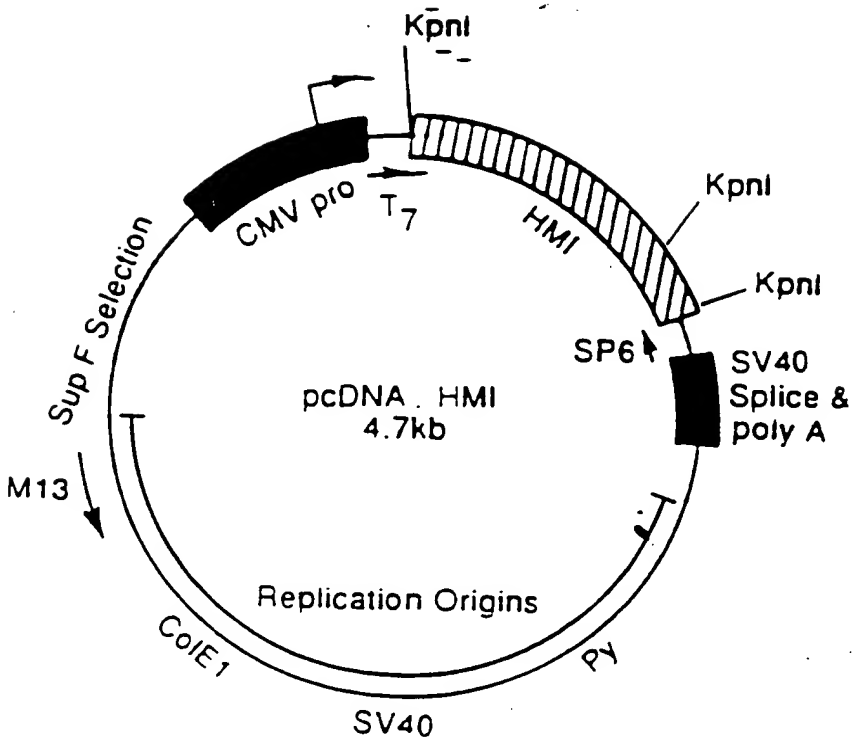

KpnI
KpnI
KpnI
CMV pro
T7
HMI
SP6
SV40
Splice &
poly A
pcDNA . HMI
4.7kb
Sup F Selection
M13
Replication Origins
ColE1
SV40
Py

FIGURE 27

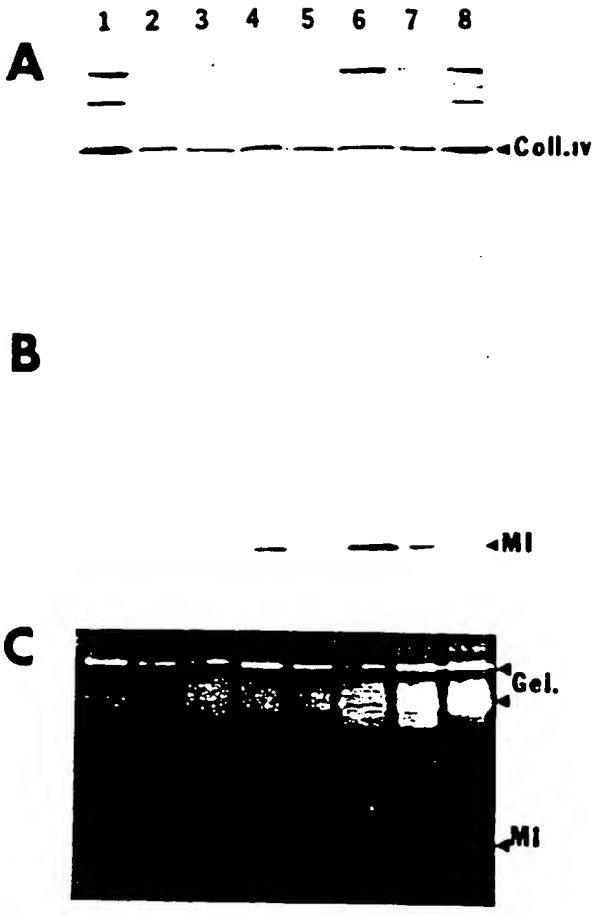


FIGURE 28

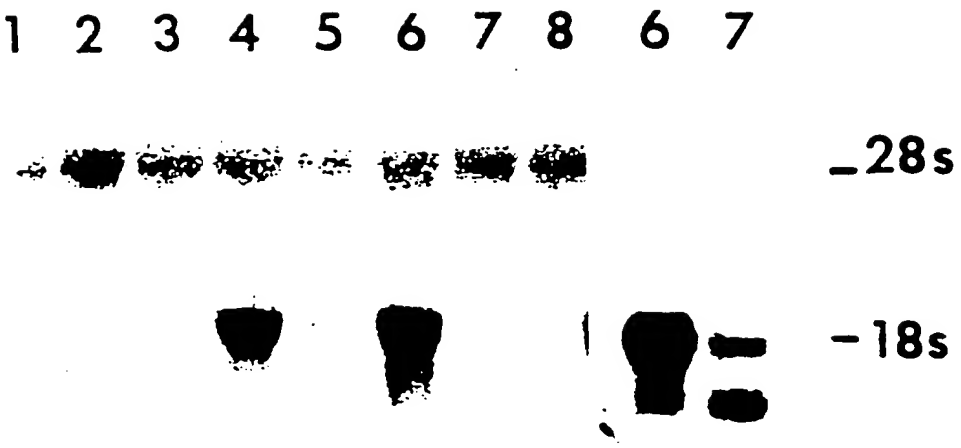


FIGURE 29

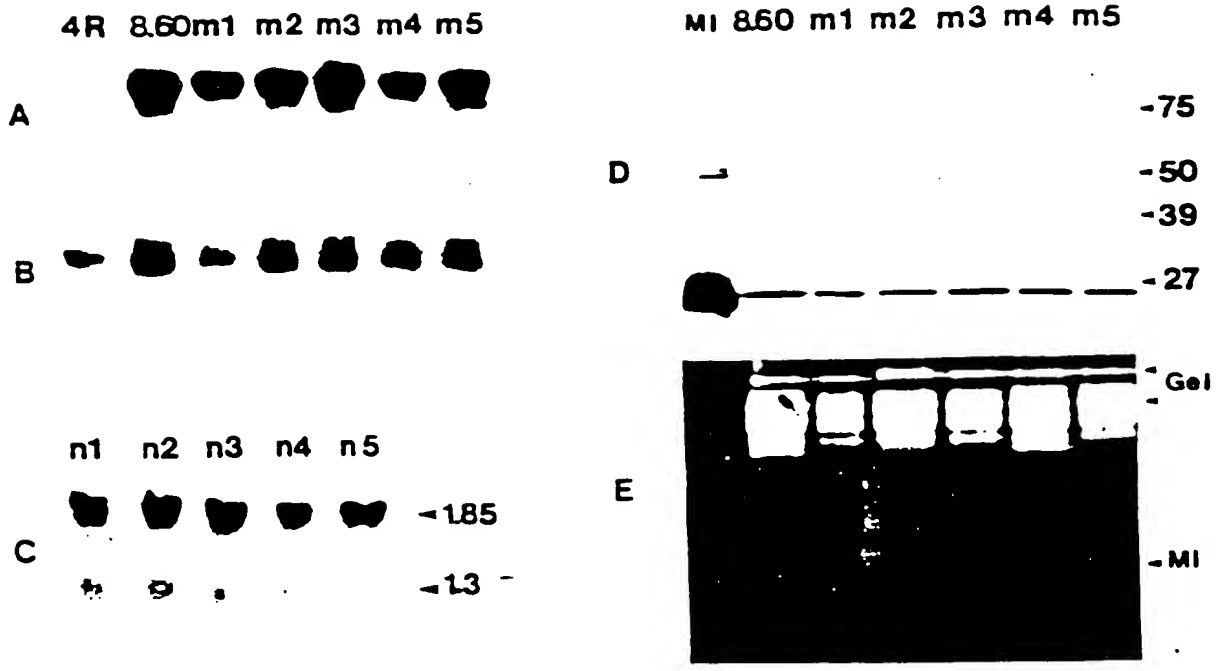

4R 8.60m1 m2 m3 m4 m5
A
B
n1 n2 n3 n4 n5
C
-1.85
-1.3
MI 8.60 m1 m2 m3 m4 m5
D
-75
-50
-39
-27
E
Gel
-MI

FIGURE 30

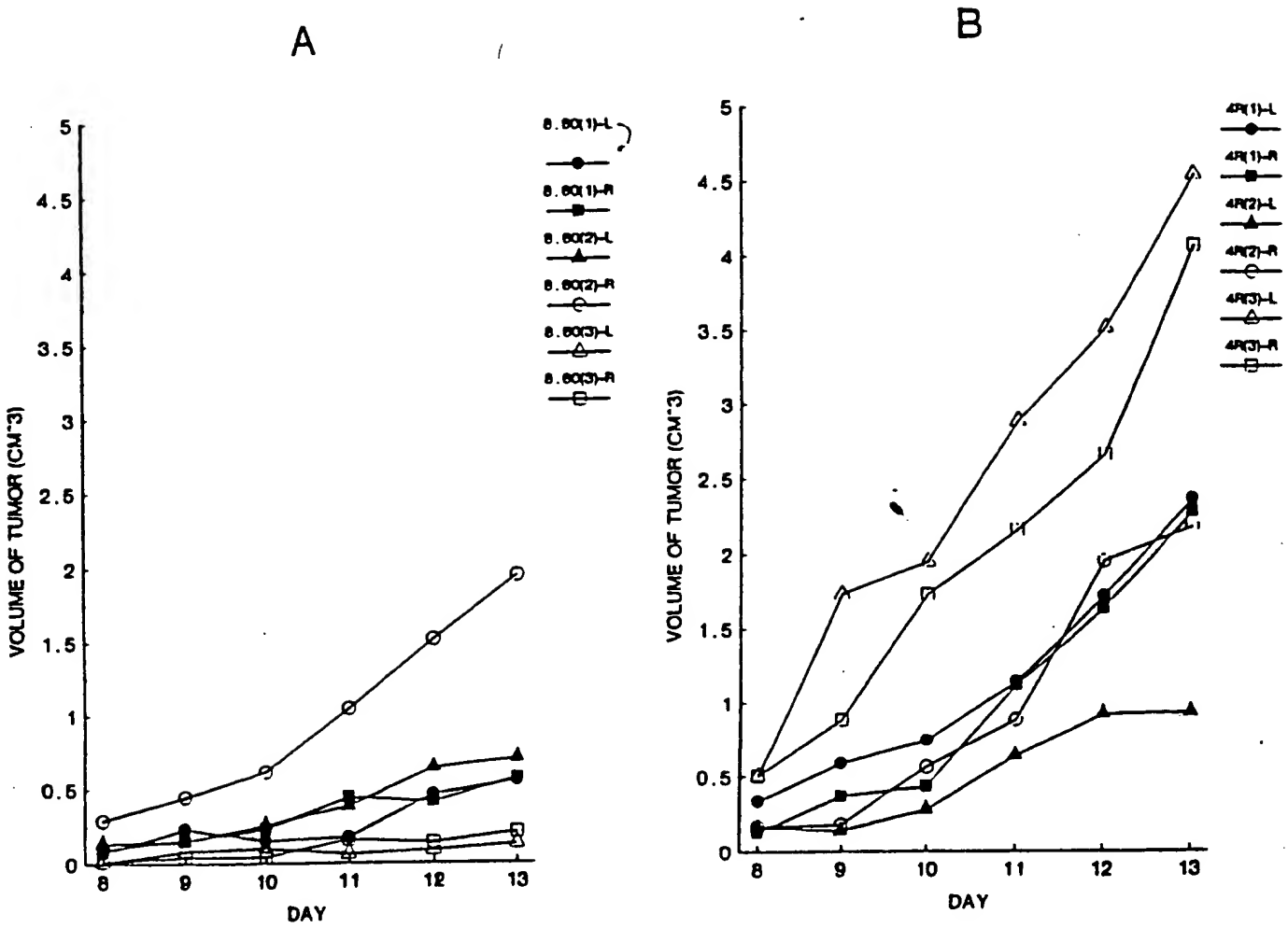

A
B
VOLUME OF TUMOR (CM^3)
DAY
8.60(1)-L
8.60(1)-R
8.60(2)-L
8.60(2)-R
8.60(3)-L
8.60(3)-R
4R(1)-L
4R(1)-R
4R(2)-L
4R(2)-R
4R(3)-L
4R(3)-R

FIGURE 31

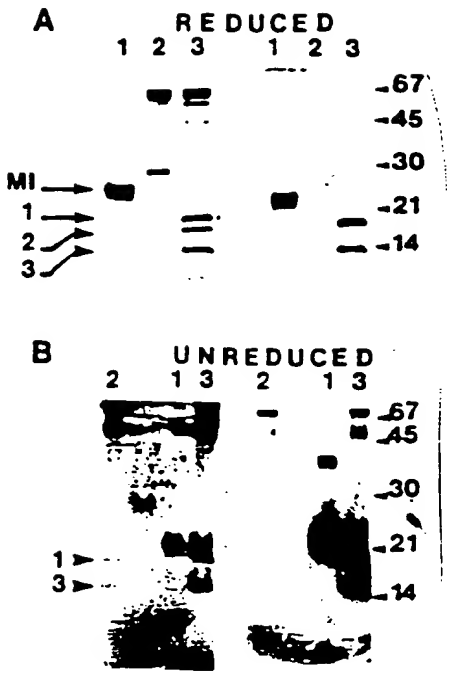

A
REDUCED
1 2 3 1 2 3
67
45
30
21
14
MI
1
2
3
B
UNREDUCED
2 1 3 2 1 3
67
45
30
21
14
1
3

FIGURE 32

Band 1: (Cys)-Ser-(Cys)-Ser-Pro-Val-His-Pro-Gln-Gln-Ala-Phe-
(Cys)-Asn-Ala-Asp-Val-Val-Ile-____

Band 2: Val-Val-Gly-Gly-Pro-(or Ala)-Val-Ala-His-Pro-His-Ser-
Trp-Pro-Thr-Gln-Val-Ser-Leu-Arg-Thr-_____

Band 3: (Cys)-Ser-(Cys)-Ser-Pro-Val-_____

FIGURE 33

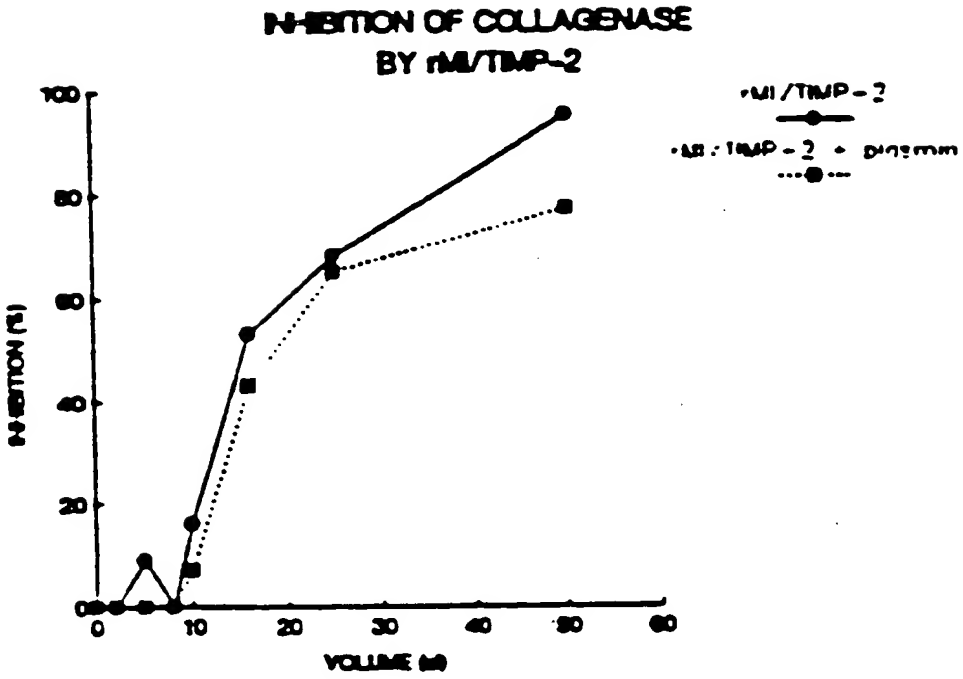

INHIBITION OF COLLAGENASE
BY rMI/TIMP-2
rMI/TIMP-2
100
80
60
40
20
0
0
10
20
30
40
50
60

FIGURE 34